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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/749,025	12/27/2000	Petrus Johannes Maria Nuijten	99511 US	6121

7590 04/05/2002

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EXAMINER
FORD, VANESSA L

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/749,025	NUIJTEN ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-11 and 14-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-11 and 14-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. This Office Action is responsive to Applicant's response in paper No. 11 to the first Office Action in paper No. 5. In response to the Amendment filed January 3, 2002, claim 4 has been cancelled. Claims 1, 2, 6 have been amended. Claims 12-16 have been added. Claims 12-16 have been renumbered 14-18 respectively, pursuant to 37 CFR 1.126.

2. In view of applicant's amendment the following Objections/Rejections are withdrawn:

a) Objection to the claims.
b) Objection to the specification.
c) Objection to the drawings.
d) Rejection of claims 2-3 and 5-7 under U.S.C. 112, first paragaraph.
e) Rejection of claims 6-7 under U.S.C. 112, second, paragraph.
f) Rejection of claims 1 and 5-6 under 35 U.S.C.102(b).
g) Rejection of claims 1-3 and 5-6 under 35 U.S.C. 102(b).
h) Rejections of claims 7-11 under 35 U.S.C. 102(b).

3. The text of those sections of the Title 35, U.S. code not included in this action can be found in the prior Office Action.

4. The rejection of claim 6, under 35 U.S.C. 35 U.S.C. 112, first paragraph is maintained, for the reasons set forth in paper 5, pages 3-6 of the previous Office Action.

The rejection was on the grounds that it is not clear that cell lines possessing the properties of *Salmonella* strain 108955 are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the claims require the use of a suitable deposit for patent purposes a deposit in a public repository is required. Without a publicly available deposit of the above *Salmonella* strain 108955, one of ordinary skill in the art could not be assured of the ability to

practice the invention as claimed. Exact replication of the cell line is an unpredictable event.

Applicant's does not refer to a deposit of *Salmonella* strain 108955 in the specification, therefore there is no assurance that all required deposits have been made and all the conditions of 37 CFR 1.801-1.809 have been met.

If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by the International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application. These requirements are necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of the deposit and the complete name and full street address of the depository is required. If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in the public repository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the repository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;
2) The name and address of the depositor;
3) The date of deposit;
4) The identity of the deposit and the accession number given by the depository;
5) The date of the viability test;
6) The procedures used to obtain a sample if test is not done by the depository; and
7) A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the *Salmonella* strain 108955 described in the claims as filed is the same as that deposited in the depository. Corroboration may take the form of a showing a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundack, 773 F.2d.1216, 227 USPQ (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Applicant urges that the Applicant's have amended the specification to refer to the address of the *Centraalbureau voor Schimmelcultures* and that a unsigned Budapest Treaty declaration has been submitted. The Applicant further states that a signed declaration will be forwarded upon receipt and that the withdrawal of this rejection is requested.

It is the Examiner's position that the rejection of claim 6 is being maintained because the Applicant has not provided the signed documents that are necessary to obviate this rejection. It should be noted that the amendment to the specification to included the address of the *Centraalbureau voor Schimmelcultures* has been entered.

5. In view of the applicant's amendment the rejection of claim 4 under 112, second paragraph is moot. Claim 4 has been cancelled.

6. In view of applicant's amendment the rejections of claim 4 under U.S.C. 102(b) are moot. Claim 4 has been cancelled.

NEW GROUNDS OF REJECTION NECESSIATED BY AMENDMENT

Claim Objections

Claim 14 is objected to because of the following informalities: What appears to be typographical errors. Claim 14 recites "tyhpi" which should be "typhi". Correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-3, 6-7 and 11 are rejected under 35 U.S.C. 102(a) as anticipated by Allen-Vercoe et al *(Epidemiol Infect, June 1999, 122(3):395-402).*

Claims 1-3, 6-7 and 11 are drawn to a mutated bacterium selected from the group consisting of *Salmonella* species *typhimurium, enteritidis, choleraesuis, dublin, abortus-ovi, abortus-equi, derby, habar, heidelberg, agona* and *arizonae* that in its wild

type form carries flagella and said mutated bacterium lacking at least one antigenic determinant of flagellin or flagella found in its wild form.

Allen-Vercoe et al teach a *Salmonella enteritidis* mutated bacterium that in its wild type form carries flagella and said mutated bacterium lacking at least one antigenic determinant of flagellin or flagella found in its wild form. Allen-Vercoe et al teach that isolated bacterial colonies were diluted using phosphate buffered saline and the inocula were administered immediately (page 396, 2nd column). Limitations such as the vaccine in a freeze-dried or spray-dried form are being viewed as process limitations.

Since the Office does not have the facilities for examining and comparing applicant's mutated bacterium with the mutated bacterium of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e.,that the mutated bacterium of the prior art does not possess the same material structural and functional characteristics of the claimed mutated bacterium). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

8. Claims 1-3 and 5-11 are rejected under 35 U.S.C. 102(b) as anticipated by Marjarian et al *(WO8910967, published November 1989).*

Claims 1-3 and 5-11 are drawn to a mutated bacterium selected from the group consisting of *Salmonella* species *typhimurium, enteritidis, choleraesuis, dublin, abortus-ovi, abortus-equi, derby, habar, heidelberg, agona* and *arizonae* that in its wild type form carries flagella and said mutated bacterium lacking at least one antigenic determinant of flagellin or flagella found in its wild form.

Marjarian et al teach the use of a live attenuated *Salmonella dubin* strain (SL5927) that is non-flagellated (and thus non-motile) and lacks at least one antigenic determinant of flagellin or flagella found in its wild form (pages 59 and 66-67). Marjarian et al teach that strain SL5927 comprises a plasmid containing a foreign epitope (i.e. SL5928)(pages 68). Marjarian et al teach that rabbits were immunized with SL5928 (i.e non-flagellated and thus non-motile) comprising a plasmid containing a foreign epitope (pages, 79-80). Marjarian et al teach that oral adminstration of the live attenuated *S. dublin* SL9528 expressing the hydrid flagella were carried out in rabbits,mice and guinea pigs (page 81). Marjarian et al teach that vaccine used in the invention are formulated with adjuvants (page 4). Limitations such as the vaccine in a freeze-dried or spray-dried form is being viewed as process limitations.

Since the Office does not have the facilities for examining and comparing applicant's mutated bacterium with the mutated bacterium of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e.,that the mutated bacterium of the prior art does not possess the same material structural and functional characteristics of the claimed mutated bacterium). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

9. Claims 14, 16 and 18 are rejected under 35 U.S.C. 102(b) as anticipated by Anderson *(GB Patent No. 1,109,179 published April 10, 1968, The London Patent Office)*.

Claims 14, 16 and 18 are drawn to a vaccine for the protection of a subject against Salmonellosis comprising an immunologically effective amount of a mutated bacterium selected from the group consisting of the *Salmonella* species *typhi* and *paratyphi* A and B that in its wildtype form carries flagella, said mutated bacterium lacking at least one antigenic determinant of flagellin or flagella found in its wildtype form or an antigenic material thereof and a pharmaceutically acceptable carrier.

Anderson teaches stable non-motile strains of *Salmonella typhi* and *Salmonella paratyphi* (A and B) which are devoid of flagella capable of producing theTH, AH or BH antibodies (p. 1, lines 51-55). Anderson teaches vaccines comprising the non-motile strains of *Salmonella typhi* and *Salmonella paratyphi* (A and B). Anderson teaches that the vaccine was rinsed with saline and administered in mucin (p. 3, lines 105-115). Anderson teaches that the vaccines can be used (p. 2, lines 50-52).

Since the Office does not have the facilities for examining and comparing applicant's *Salmonella* vaccine with the *Salmonella* vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e.,that the *Salmonella* vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed *Salmonella* vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

10. Claims 14-18 are rejected under 35 U.S.C. 102(b) as anticipated by Marjarian et al *(WO8910967, published November 1989).*

Claims 14-18 are drawn to a vaccine for the protection of a subject against Salmonellosis comprising an immunologically effective amount of a mutated bacterium selected from the group consisting of the *Salmonella* species *typhi* and *paratyphi* A and B that in its wildtype form carries flagella, said mutated bacterium lacking at least one antigenic determinant of flagellin or flagella found in its wildtype form or an antigenic material thereof and a pharmaceutically acceptable carrier.

Marjarian et al teach recombinant flagellin vaccine formulations (see the Title). Marjarian et al teach attenuated invasive bacteria expressing the recombinant flagellin genes of the invention used in live vaccine formulations (see the Abstract). Marjarian et al teach that the coding region from the H1-d flagellin gene is present in a 3.8 kb EcoRI genomic fragment and contains two restriction sites and that an additional *Eco*RV site is present. Marjarian et al teach that two subclones were constructed by the insertion of the 3.8 kb genomic fragment into the *Eco*RI site. Marjarian et al teach that a 51 bp *Eco*RV fragment was deleted from each of the subclones which resulted in a unique *Eco*RV restriction site available for insertion of oligonucleotides specifying a foreign epitope (page 14 and Figure 1). Marjarian et al teach that recombinant flagellin proteins are exported to the cell surface where they assemble into functional flagella containing the heterologous (foreign) epitope. Marjarian teach that recombinant flagellin fusion proteins provoke a cellular, mucosal or humoral response (page 11). Marjarian et al teach that *Salmonella* species which in attenuated forms can be used in the vaccine formulations of this invention are *S. typhi, S, typhimurium, S. paratyphi A, S. paratyphi B*

and S. enteritidis serotype dublin (Table II, page 40 and claim 41, page 104). Marjarian et al further teach that the vaccine formulations of their invention are often formulated and inoculated with various adjuvants. Marjarian et al teach examples of suitable adjuvants include Freund's adjuvant (complete or incomplete), Adjuvant 65 (containing peanut oil, mannide monooleate and aluminum monostearate), the pluronic polyol L-121, Avridine and mineral gels such as aluminum hydroxide and aluminum phosphate (page 4-5). Limitations such as the vaccine in a freeze-dried or spray-dried form is being viewed as process limitations.

Since the Office does not have the facilities for examining and comparing applicant's *Salmonella* vaccine with the *Salmonella* vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e.,that the *Salmonella* vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed *Salmonella* vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Pertinent Prior Art

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure Allen-Vercoe et al *(Vet Microbiol. September 29,1999;69(4):265-275 and U.S. Patent 6,130,0982, published October 10, 2000).*

Status of Claims

12. No claims are allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
March 27, 2002

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